

Catalytic Ring-Closing Olefin Metathesis of Sulfur-Containing Species: Heteroatom and Other Effects

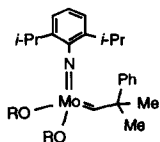
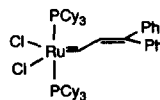
Young-Seok Shon and T. Randall Lee*

Department of Chemistry, University of Houston, Houston, TX 77204-5641

Abstract: This paper describes studies of the ring-closing metathesis of dialkyl sulfides and disulfides catalyzed by molybdenum and ruthenium alkylidenes. In general, the highest yields of ring-closed products were obtained using the molybdenum catalysts. Product yields were also strongly influenced by the substitution pattern about the double bonds: the yield of ring-closed products was found to decrease as the degree of substitution increased. These effects and other heteroatom effects are discussed. © 1997 Elsevier Science Ltd. All rights reserved.

The ring-closing metathesis (RCM)¹ of olefinic ethers,² esters,³ amines,^{4,5} thioethers,^{6,7} and allylic phosphanes⁸ has been accomplished using various catalytic systems based on Mo, W, Re or Ru. To our knowledge, however, the metathesis of disulfide-containing species has not been reported. Our initial interest in studying the RCM reactions of these species was spurred by our desire to use RCM to prepare cyclic unsaturated disulfides for use in generating new types of chelating self assembled monolayers (SAMs) on gold.⁹ In addition, we believed that the development of new synthetic strategies involving sulfur-containing molecules should benefit from the availability of this reaction.

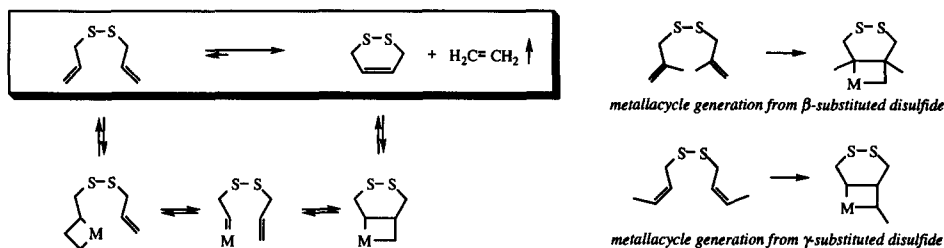
Schrock et al. synthesized a highly active molybdenum imido alkylidene **1** that catalyzes the ring opening metathesis polymerization (ROMP) of strained cyclic olefins.¹⁰ This catalyst has been used to prepare a number of heterocycles via the ring-closing metathesis of olefinic ethers,² esters,³ and amines.^{4,5} More recently, Grubbs et al. synthesized the ruthenium alkylidene **2**, which is not only highly active in RCM reactions, but also highly tolerant of polar functional groups and protic media.¹¹ Given the exceptional RCM activities of complexes **1** and **2**, we chose to study these catalysts in the metathesis of a series of acyclic diene disulfides and related molecules.


 1 R = CMe(CF₃)₂


2 Cy = Cyclohexyl

The catalytic ring-closing olefin metathesis strategy is illustrated in Scheme 1 for the synthesis of unsaturated disulfide heterocycles from acyclic diene disulfides. Catalyst **1** effects the cyclization of a

Scheme 1



wide range of dienes to afford the desired disulfide heterocycles in widely varying yields (Table 1). By comparison, catalyst **2** is generally less effective.¹²

Examination of the RCM of a series of dienes that contain different heteroatoms reveals that oxygen-containing substrates give the highest RCM yields, and that disulfide-containing substrates give the lowest. The relatively poor yields observed for the RCM of disulfide-containing substrates probably originate from two factors: the additional torsional strain in the heterocycle imposed by the preferred 90° dihedral angle of the disulfide moiety,¹³ and poisoning of the catalyst by the disulfide moiety (particularly in the case of catalyst **2**). The ring-closing metathesis of diallyl ether in the presence of disulfide and secondary amine groups (entries 12 and 13, respectively) indicates that the secondary amine is the least tolerated of the functional groups examined here: catalyst **1** appears to be strongly poisoned by the amine but not the disulfide; catalyst **2** appears to be strongly poisoned by both of these functional groups.

The influence of sterics on the RCM of acyclic diene disulfides is illustrated by entries 1-5. In reactions catalyzed by **1**, two significant trends can be noted. First, substitution γ to the sulfur atom inhibits the RCM reaction (entry 1 vs. entry 2). Second, substitution β to the sulfur atom shows an even more pronounced inhibition (e.g., entry 1 vs. entry 3); in fact, bis(2-methyl-2-propenyl) disulfide fails to undergo RCM at all (entry 5). These results highlight the difficulty in forming tri- and tetra-substituted double bonds using the RCM strategy. Since more highly substituted olefins are generally more thermodynamically stable than less substituted olefins, the observed trend in reactivities is probably influenced by kinetic parameters. This kinetic preference might originate from the fact that metallacycles generated from β -substituted disulfides are more sterically crowded than those generated from γ -substituted disulfides (e.g., Scheme 1). It is possible, however, that the reaction steps that precede formation of the sterically crowded metallacycle are responsible for the observed differences.

Acknowledgments: Support for this research was provided by the Camille and Henry Dreyfus Foundation (New Faculty Award to TRL; NF-93-040), the National Science Foundation (CAREER Award to TRL; CHE-9625003), and the Robert A. Welch Foundation (Grant No. E-1320). Acknowledgment is made to the donors of The Petroleum Research Fund, administered by the ACS, for partial support of this research (ACS-PRF# 30614-G5). We thank our colleagues Eric Dias and Jonathan Friedman for helpful comments.

Table 1. Catalytic Ring-Closing Metathesis of Acyclic Dienes (10 mol % **1** or **2**, C₆D₆, 20 °C)^{14, a}

entry	substrate	product	catalyst 1		catalyst 2	
			time (h)	yield (%)	time (h)	yield (%)
1			1	77	3	0
			24	76		
			1	9 ^b		
			3	54	3	0
2			3	54	3	0
3			3	15	3	0
4			3	11	3	0
5			12	0	12	0
6			1	99	24	29
			1	99 ^b	24	25 ^b
7			1	97 ^b (94)	3	0
8			1	99	1	99 ^b
			1	99 ^b		
			1	96 ^b (91)	3	69 ^b
9			1	96 ^b (91)	24	90 ^b
10			2	58	3	0
			24	82		
			24	17 ^b		
11			3	92 ^b (84)	3	3 ^b
12			1	99	1	2
			24	99		
			1	27		
			1	34	1	0
			24			
13			1	7	1	0
			24	8		
			1	17		
			24	28	1	0

^a Yields reported for newly examined substrates and competition experiments (entries 1-5, 7, 10, 12, 13) are the average of at least two runs. The observed yields varied by no more than $\pm 6\%$ from the average. Yields reported for previously examined substrates (entries 6, 8, 9, 11) are consistent with those reported in the literature.^{2,4,6} Yields were determined by ¹H NMR. Isolated yields are shown in parentheses. ^b 5 mol % **1** or **2**.

References and Notes

- For reviews, see: Grubbs, R.H.; Miller, S.J.; Fu, G.C. *Acc. Chem. Res.* **1995**, *28*, 446; Schmalz, H. *Angew. Chem. Int. Ed. Engl.* **1995**, *17*, 34.
- Fu, G.C.; Grubbs, R.H. *J. Am. Chem. Soc.* **1992**, *114*, 5426.
- Sibejin, M.; Mol, J.C. *Appl. Catal.* **1991**, *67*, 279.
- Fu, G.C.; Grubbs, R.H. *J. Am. Chem. Soc.* **1992**, *114*, 7324.
- Larroche, C.; Laval, J.P.; Lattes, A.; Basset, J.M. *J. Org. Chem.* **1984**, *49*, 1886.
- O'Gara, J.E.; Portmess, J.D.; Wagener, K.B. *Macromol.* **1993**, *26*, 2837.
- Lefebvre, F.; Leconte, M.; Pagano, S.; Mutch, A.; Basset, J.-M. *Polyhedron* **1995**, *22*, 3209.
- Leconte, M.; Isabelle, J.; Pagano, S.; Lefebvre, F.; Basset, J.-M. *J. Chem. Soc., Chem. Commun.* **1995**, 857.
- For reviews of SAMs, see: Whitesides, G.M.; Laibinis, P.E. *Langmuir* **1990**, *6*, 87; Ulman, A. *An Introduction to Ultrathin Organic Films*; Academic: San Diego, 1991; Ulman, A. *Chem. Rev.* **1996**, *96*, 1533.
- Fox, H.H.; Yap, K.B.; Robbins, J.; Cai, S.; Schrock, R.R. *Inorg. Chem.* **1992**, *31*, 2287; Schrock, R.R.; Murdzek, J.S.; Bazan, G.C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875.
- Fu, G.C.; Nguyen, S.T.; Grubbs, R.H. *J. Am. Chem. Soc.* **1993**, *115*, 9856.
- A more active version of **2**, where the alkylidene is a benzylidene, has recently been reported: Schwab P.; France, M.B.; Ziller, J.W.; Grubbs, R.H. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2039; Schwab, P.; Ziller, J.W.; Grubbs, R.H. *J. Am. Chem. Soc.* **1996**, *118*, 100. Preliminary experiments in our laboratories suggest that this Ru-based catalyst also fails to catalyze the RCM of the acyclic disulfides reported in Table 1.
- Burns, J.A.; Whitesides, G.M. *J. Am. Chem. Soc.* **1990**, *112* 6296, and references therein.
- Experiments were performed under an inert atmosphere in an Innovative Technologies glovebox, or by using standard Schlenk techniques. Benzene-*d*₆ and reagent grade benzene were dried by passage through activated alumina, and degassed using the Freeze-Pump-Thaw method. Diallyl amine, diallyl disulfide, diallyl ether and diallyl sulfide were purchased from Aldrich Chemical Co., and were of the highest purity available. Diallyl amine was further purified by chromatography on silica gel, and degassed before use. Diallyl disulfide was distilled, purified by chromatography on silica gel, and degassed before use. Diallyl ether and diallyl sulfide were simply degassed before use. The other substrates reported in Table 1 were synthesized, purified and characterized by established methods, and degassed before use. Catalytic RCM reactions were conducted and analyzed as described below.
Typical NMR Tube Reaction. Diallyl disulfide (5.4 mg, 0.037 mmol) in 0.5 mL of dry C₆D₆ containing an aliquot of ferrocene (used as an internal standard for ¹H NMR integrations) was added to a homogeneous yellow solution of **1** (2.7 mg, 0.0037 mmol) in 0.5 mL of dry C₆D₆ under an atmosphere of nitrogen. The reaction mixture was transferred to well sealed NMR tube. At the indicated intervals of time shown in Table 1, ¹H NMR spectra were obtained, and the yields were calculated by integration relative to the internal standard.
Typical Bulk Reaction. Allyl 1-phenyl-3-butenyl ether (0.115 g, 0.613 mmol) was added to a homogeneous yellow solution of **1** (0.0233 g, 0.0307 mmol) in 15 mL of dry C₆H₆ under argon. The resulting mixture was stirred at 20 °C for 1 h. The reaction mixture was quenched by the addition of water, extracted (1 N HCl/Et₂O), dried over MgSO₄, filtered, and evaporated. Chromatography of the concentrated solution on silica gel (1:49, ethyl acetate:hexane) afforded 0.0897 g (91% yield) of the ring-closed compound as a colorless oil.

(Received in USA 23 August 1996; revised 3 January 1997; accepted 6 January 1997)